Death from cumulative sodium stibogluconate toxicity on Kala-Azar

Pentavalent antimonial compounds are the most widely used drugs for the treatment of leishmaniasis, but side-effects are frequent [1].

We report the case of a 4-year-old-male who was diagnosed with visceral leishmaniasis after examination of a bone marrow biopsy. The patient was started on 20 mg/kg intravenous sodium stibogluconate daily (1200 mg/day) and 16 mg/kg oral allopurinol daily (100 mg three times daily). This regimen was supplemented with albumin and blood. On day 3, he reported chest pain and persistent cough, and the drugs were withdrawn. Electrocardiography (ECG) was unremarkable at that time. Three days after the treatment had been discontinued, petechial rashes were seen on the lower extremities. Sepsis and other causes of petechial rash were ruled out. Three days after treatment was discontinued, the patient was found dead in bed. ECG showed ventricular fibrillation.

Sodium stibogluconate with a valency of 5+ and meglumine antimonate are used in the treatment of leishmaniasis [1]. Stibogluconate sodium (Pentostam) is the term used in English-speaking countries, including the USA. Sodium stibogluconate solution contains about 10% pentavalent antimony (100 mg/mL) [1]. Side-effects include abdominal pain, vomiting, nausea, fatigue, headache, increase of liver enzymes, nephrotoxicity, arthralgia, fever, rash, cough, pneumonia, pancytopenia and reversible peripheral neuropathy. Recent studies suggest that elevations of amylase and lipase are common, and that a subset of patients suffer clinically significant pancreatitis. Nonetheless, these side-effects rarely lead to discontinuation of the drug [2–4].

Dose-related changes in ECG can also be seen. Nevertheless, serious side-effects, such as atrial and ventricular arrhythmia, atrial fibrillation, ventricular tachycardia, ventricular fibrillation, and torsade de pointes, are rare. Torsade de pointes induced by pentavalent antimony, followed by sudden death, has been observed [3–5]. Arrhythmias and sudden death have been reported with doses greater than 20 mg/kg body weight/day [1]. Administration of the drug at normal doses rarely results in the death of patients. It should be kept in mind that pentavalent antimony is contraindicated in patients with myocarditis, hepatitis and pancreatitis [6,7].

Even the normal dose of sodium stibogluconate can lead to both cardiotoxicity and hematotoxicity, because of its cumulative effects. These side-effects may occur even after the drug is withdrawn, as in our case. We therefore suggest that patients with leishmaniasis who are being treated with antimony compounds be observed cautiously for signs of cardiologic and hematologic changes.

S. Cesur*, K. Bahar and S. Erekul
Ankara Üniversitesi Týp Fakültesi Ýnfeksiyon Hastalýklarýve Kinik Bakteriyoloji,
Anabilim Dalý Sýhhiye,
06100 Sýhhiye-Ankara,
Turkey
*Tel: +90 312 3103333
E-mail:scesur89@yahoo.com

REFERENCES

1. Pearson DR, Sousa De Queiroz A. Leishmania species: visceral (Kala-azar), cutaneous, mucosal leishmaniasis. In: Mandell G, Bennett EJ, Dolin R, eds. *Principles and practice of infectious diseases*, 4th edn. New York: Churchill Livingstone, 1995. 2428–2442.
2. Hepburn NC, Tidman MJ, Hunter JA. Aminosidine versus sodium stibogluconate for the treatment of American cutaneous leishmaniasis. *Trans R Soc Trop Med Hyg* 1994; 88: 700–3.
3. Thakur CP, Sinha GP, Pandey AK *et al.* Do the diminishing efficacy and increasing toxicity of sodium stibogluconate in the treatment of visceral leishmaniasis in Bihar, India, justify its continued use as a first drug? An observational study of 80 cases. *Ann Trop Med Parasitol* 1998; 92: 561–9.
4. Ortega-Carnicer J, Alcazar R, De la Torre M *et al.* Pentavalent antimonial-induced torsade de pointes. *J Electrocardiol* 1997; 30: 143–5.
5. Berman JD. Human leishmaniasis: clinical, diagnostic and chemotherapeutic development in the last 10 years. *Clin Infect Dis* 1997; 24: 684–703.
6. Donovan KL, White AD, Cooke DA *et al.* Pancreatitis and palindromic arthropathy with effusions associated with sodium stibogluconate treatment in renal transplant recipient. *J Infect* 1990; 21: 107–10.
7. Halim MA, Alfurayh O, Kalin ME *et al.* Successful treatment of visceral leishmaniasis with allopurinol plus ketoconazole in renal transplant recipient after the occurrence of pancreatitis due to stibogluconate. *Clin Infect Dis* 1993; 16: 379–9.